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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/699,465	10/31/2003	Marlon D. Cowart	6789.US.D1	2713

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EXAMINER	
BERNHARDT, EMILY B	

ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 05/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/699,465	COWART ET AL.	
	Examiner	Art Unit	
	Emily Bernhardt	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-58 and 65-112* is/are pending in the application.

4a) Of the above claim(s) *1-58,65-89 and 103-112* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *90-92,94-96,98,100 and 101* is/are rejected.

7)☒ Claim(s) *93,97,99 and 102* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/31/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Consistent with parent, restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-40 and 65-70, drawn to method for treating female sexual dysfunction (SD) where Z=N, classified in class 514, subclasses 252.19,329,333 and others as determined by the nature of the "Z" and/or "A" ring.

II. Claims 1-40, drawn to method for treating male sexual dysfunction (SD) where Z=N, classified in class 514, subclasses 252.19,329,333 and others as determined by the nature of the "Z" and/or "A" ring.

III. Claims 41-46, drawn to method for treating SD employing various compounds of in combination with PDE V inhibitors, classified in class 514, subclasses various as determined by the exact nature of active ingredients employed.

IV. Claims 47-52, drawn to method for treating SD employing various compounds and α adrenergic agents , classified in class 514, subclasses various as determined by the exact nature of active ingredients employed.

V. Claims 53-58, drawn to a method for treating SD employing compounds in combination with dopamine agonists, classified in class 514,

subclasses various as determined by the exact nature of active ingredients employed.

VI. Claims 71-89, drawn to additional uses employing various compounds, classified in class 514, subclass 252.19,etc. and many other subclasses based on the nature of X and/or A rings.

VII. Claims 90-102 , drawn to compounds where A= first row in claim 90 and 1st ring of 2nd row in claim 90 and pyridyl in claim 94,etc., classified in class 544, subclasses 295,364,370.

VIII. Claims 90 and 93, drawn to compounds not provided for by VII- i.e. A= remaining rings in 2d through 4th rows, classified in class 544, subclasses such as 366,367 and 369.

IX. Claims 103-109, drawn to compounds where Z=CH, classified in class 546, subclass 199,etc. and others as determined by the nature of the A ring.

X. Claims 103 and 110-112, drawn to compounds where Z=C, classified in class 546, subclass 273.4,etc. and others as determined by the nature of the A ring.

If one of groups III-V is elected, applicants must elect a species within formula (I) and a and a single species as the co-ingredient.

If Group VI is elected applicants must pick a single use for examination. Further restriction may be required at Z/A if Groups I-VI are elected. If VIII/IX is elected further restriction may be required at A by the receiving examiner.

The inventions are distinct, each from the other because of the following reasons: Compounds within groups I-VI relate to compounds of considerable structural dissimilarity in view of the varying cores based on Z as well as variable "A" which permit a wide of variety hetero ring systems. Thus they are separately classified based at the very least on species recited in various claims. Each can support a patent as the compounds of each group are capable of being utilized alone not in combination with other members listed in the Markush group. Groups I-II are not commensurate with compound groups VII-X as the choice of A ring systems is narrower in the latter set and the search for one set of groups is not required for the remaining set as set forth above. Thus different issues of patentability may arise. Where more than one use exists restriction is also proper and thus groups VI which embraces many additional uses is distinct from that

covered in VII-X and may raise art issues for the broader scope of compounds covered than for compound groups.

Additionally, compounds employed in VII-X vs. III-V may be old or obvious when separately employed but may be patentable due to superior,or synergistic properties not present for the individual components in I-III. Within groups III-V there is more than one invention as the claims embrace multiple combinations which require independent searches and which are not art-recognized equivalents in the art.

During a telephone conversation with Ms.Ferrari-Dileo on 4/24/06 a provisional election was made with right of traverse to prosecute the invention of VII, claims 90-102. Affirmation of this election must be made by applicant in replying to this Office action. Claims 1-58 and 65-112 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be

accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

The disclosure is objected to because of the following informalities: Applicants requested insertion of most recent parent into parent history but the amendment does not follow with "which is claims priority to..." . See MPEP 1302.04. Appropriate correction is required.

Claims 90-92,94-96,98,100-101 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Nature of prodrugs intended is not known except for esters, amides exemplified in the specification on p.73 and some of the R_E choices stated to be prodrugs. A prodrug is chosen based on some undesirable property present in the parent compound and once the type of improvement is identified there is testing to determine the prodrug's efficacy and ability to regenerate the parent compound. It is not the norm that one can predict with any degree of accuracy a particular prodrug form of an active compound will be more soluble, more easily handled in formulations or more bioavailable without actual testing in vivo . Thus the design of prodrugs is far from trivial and is dependent on the undesirable properties of the active compound(s) which will vary from drug to drug. Thus in the absence of any

guidelines (none is seen in the specification) as to what type of property is to be improved/or modified it cannot be readily determined what is and what is not within the instant scope.

Claim 99 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The methyl substituent on the pyridine ring is not embraced in claim 94 from which 99 ultimately depends.

Claims 90 and 94 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specification provides no adequate support how to use **representative** scope of piperazines claimed at R_E which can carry from a reading of the specification a huge array of "heterocyclecarbonyl" groups which include mono-, bi- and tricyclic ring systems which in turn are further substituted with many more functional groups as described on p.38-39 as well as other chemical moieties. Compounds which have been made herein have R_E as H. On

p.67 of the specification it is stated that the compounds of the invention are dopamine agonists. However, there is no reasonable assurance as to what other substituents will work as there is no only test data for one compound in several tests and thus no insight into structure-activity trends that need to be evaluated. Note In re Surrey 151 USPQ 724 regarding sufficiency of disclosure for a Markush group where as herein no examples of a diverse nature have been made much less tested showing the requisite activity needed to practice the invention. Also see MPEP 2164.03 for enablement requirements in cases directed to structure-sensitive arts such as the pharmaceutical art. Also note the criteria for enablement as set out in In re Wands cited in MPEP 2164.01(a),August 2000 edition, which includes factors such as:

1) Breadth of the claims- the claims cover compounds easily in the millions as pointed out above;

2) Level of unpredictability in the art- the invention is pharmaceutical in nature involving activity at one or more dopamine receptors. It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved" and physiological activity is generally considered to be unpredictable. See In re Fisher 166 USPQ 18;

3) Direction or guidance- compounds actually made are much closer to each other than to remaining scope ;

4) State of the prior art- The compounds are benzimidazolylalkylene piperazine derivatives with varying heteroaryl rings at other nitrogen terminus. While such compounds are known in the prior art having the same activity, they are similar (if not identical) to compounds actually made and tested herein but not to generic scope covered;

5) Working examples- test data has been presented for only one compound and thus no clear evaluation of which functional groups at various positions out of the many claimed might affect potency to a large or small degree.

In view of the above considerations, this rejection is being applied.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 94,95,98-100 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sule (abstract provided). Sule describes similar compounds having anthelmintic activity. See pyridyl species attached to the abstract which was obtained from a computer-assisted search. The sole difference is that the piperazine

and/or pyridine rings . H vs 1or 2 Me's in otherwise old compounds is not considered patentable absent evidence of superior, unexpected results. Note In re Wood 199 USPQ 137; In re Lohr 137 USPQ 548; In re Fauque 121 USPQ 425. Preparation of methylated products following the teaching of Sule would be routine since methylated piperazine/pyridine reactants are readily available from many Chemical Suppliers. Thus it would have been obvious to one skilled in the art at the time the invention was made to expect compounds claimed herein that are methylated on pyridine ring or on the piperazine ring to also possess the use taught by the art in view of the close structural similarity outlined above and their preparation to be well within the ordinary skill of the art.

US'166 is made of record. While it describes many compounds within the instant scope it has the same inventive entity as herein and a too late publication date and thus is not applied. It has gone abandoned with no refilings.

Parent applications serial no. 10/094265 has been recently allowed. The claims are drawn to method of use after a restriction/election was made. A CIP (US'589) is also made of record as it drawn to method claims after a restriction/election.

Claims 93,97,99 and 102 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Emily Bernhardt whose telephone number is 571-272-0664.

If attempts to reach the examiner by telephone are unsuccessful, the acting supervisor for AU 1624, James O. Wilson can be reached at 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

E Bernhardt

Emily Bernhardt
Primary Examiner
Art Unit 1624